Imaging dynamic and selective low-complexity domain interactions that control gene transcription.

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Public Summary:
Many eukaryotic transcription factors (TFs) contain intrinsically disordered low-complexity sequence domains (LCDs), but how these LCDs drive transactivation remains unclear. We used live-cell single-molecule imaging to reveal that TF LCDs form local high-concentration interaction hubs at synthetic and endogenous genomic loci. TF LCD hubs stabilize DNA binding, recruit RNA polymerase II (RNA Pol II), and activate transcription. LCD-LCD interactions within hubs are highly dynamic, display selectivity with binding partners, and are differentially sensitive to disruption by hexanediols. Under physiological conditions, rapid and reversible LCD-LCD interactions occur between TFs and the RNA Pol II machinery without detectable phase separation. Our findings reveal fundamental mechanisms underpinning transcriptional control and suggest a framework for developing single-molecule imaging screens for drugs targeting gene regulatory interactions implicated in disease.

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